EXHIBIT 1

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FUJIFILM

Application Note

SCIENCE IMAGING SYSTEMS

Application Note No.26

In Vivo Imaging of Tumor-Bearing Nude Mouse with DY-676 Labeled Monoclonal Antibody Using Near-Infrared Light

LAS-4000

Foreword

Optical molecular imaging is rapidly becoming the tool of choice for localization of in vivo targets such as tumors, lesions or stem cells. Fluorescent organic molecules such as Indocyanine green, as well as semiconductor materials such as nanocrystal quantum dots, have greatly facilitated the use of cost effect planar imaging systems for elucidating targets in small animals. Cooled CCD cameras can easily be used to shed light on the mass and location of expressed phenotypes in animal models longitudinally reducing the need to sacrifice larger groups of animals at various time points. In the present study, we report the use of LAS-4000 IR multi color fluorescence imaging system for detection of targeted fluorescence in a tumor-bearing nude mouse model. A monoclonal antibody labeled with a near-infrared (IR) probe was easily detected with very low background using LED illumination. The images in this study were generously provided by Perseus Proteomics Inc. (Tokyo, Japan)

Contents

Summary

- Low background in vivo imaging of a tumor-bearing nude mouse was performed using near IR LED illumination.
- Automated operation of the LAS-4000 IR multi color imager, using the in vivo mode, produced optimized images of both brightfield (digitized image using white LED's) and antibody targeted near IR fluorescence.
- Individual images were automatically superimposed to allow for visual confirmation of tumor localization.

1 Introduction

In vivo optical imaging is an emerging detection technology that allows an investigator to evaluate the timing, location and in some cases the function, of a variety of small molecules and proteins in a single live animal longitudinally. There are currently a variety of fluorescent and luminescent labels that can be employed depending on the target to be localized. One technique that is becoming increasing popular is the use of antibodies, targeted at cell surface markers, to identify tumors in vivo. In the following experiment, an antibody labeled with near-infrared dye (DY-676, Dyomics GmbH) was administered to a tumor-bearing nude mouse that was then subjected to imaging with near-infrared light. Major advantages of this fluorescence imaging methodology include faster detection times (i.e. average exposure times are on the order of seconds as opposed luminescence imaging exposures which can take up to 30 minutes), and multi-spectral capabilities (i.e. the ability to look at multiple dyes from the same target). Fluorescence imaging in the near IR region provides the additional advantages of low background (i.e. less auto-fluorescence in the near IR region) and deeper signal localization (i.e. excitation and emission wavelengths in the near IR have higher tissue penetration than lower visible wavelengths). These properties address two of the primary problems that have been associated with in vivo fluorescence imaging of targets within small animals. In the present study detection of the accumulated DY-676 labeled antibody (which is targeted at a tumor cell surface marker) was performed using LAS-4000 IR multi color imager equipped with near IR LED's (i.e. peak wavelength 710 nm) for epi-illumination and a 785 nm long pass emission filter. The near IR LED's are also equipped with white LED light to facilitate generation of brightfield images. Finally, the workflow for producing the overlaid near IR image and digital images using FUJIFILM's MultiGauge software is described.

2 Experimental Methods

Label using DY-676 Monoclonal Antibody

1) Gently mix 1 ml of the 5 mg/ml antibody solution (dissolve in 50 mM sodium hydrogen carbonate buffer, pH 8.5, containing 0.5 M NaCl) with 2.5 µl of 25 mM DY-676-NHS Ester dissolve in dimethylformamide (supplied by Dyomics) The molar reaction ratio of antibody/DY-676 = 1 : 2.
2) React (protect from light) for 1 hour at room temperature (about 25℃).
3) Place the sample in a PD-10 desalting column (GE Healthcare Bioscience) that has been previously equilibrated using 20 mM sodium phosphate buffer, 150 mM NaCl, pH 7.2, and pool the high molecular weight fraction.
4) Measure the absorbance of the pooled fraction at 280 nm and 674 nm, and calculate the concentration of the antibody and the binding number of the fluorescent-labeled molecule per molecule of antibody.
   (1) Molar absorbance coefficient of antibody (at 280 nm, molecular weight 150,000) : 220,000 $M^{-1}cm^{-1}$
   (2) Molar absorbance coefficient of DY-676 (at 674 nm, molecular weight 906) : 145,000 $M^{-1}cm^{-1}$
5) Store the sample in an opaque tube at -20℃ until needed.

Antibody: Antibody targeted at the human tumor cell surface marker (supplied by Perseus Proteomics Inc.) http://www.ppmx.com

Note : In the present experiment the average molecular binding number of DY-676 per molecule of antibody was approximately 0.8.

The Tumor-Bearing Mouse

1) Create a tumor-bearing mouse model by subcutaneously injecting (1 x 10^7 cells/ mouse) the lateral side of the nude mouse with the human tumor cell strain that expresses the molecule to which the aforementioned monoclonal antibody reacts.
2) Immobilize the tumor-bearing mouse using Isoflurane or other approved anesthetic.
3) Intravenously administer 0.1 ml of normal saline diluted DY-676 labeled antibody (antibody concentration : 5 mg/ml) to the tail vein of the tumor-bearing mouse.

3 Imaging Method

Imaging using LAS-4000 IR multi color imager

Inject DY-676 and after 24hours, position the animal on the tray with head juxtaposed to the nosecone and the tumor facing upward toward the camera.

1) Select the "in vivo" mode* (1) as the "Exposure Type" (Fig.1).

* The "in vivo" mode displays superimposed images detected by white LED and near infrared (IR) light.

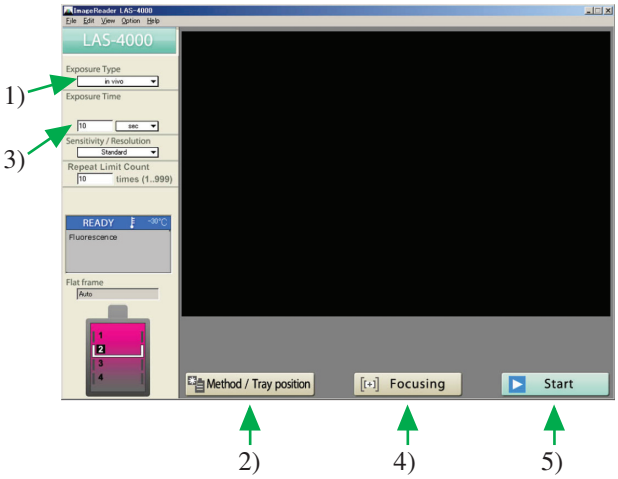

Fig.1 LAS-4000 IR multi color image

2) Click the "Method/Tray Position" button (2), select "Fluorescence" as the "Method", and select the "Tray Position" suitable for the sample size.
3) Enter the Exposure time (3) and the "Repeat Limit Count" to set the total number of images to be acquired.
4) Click the "Focus" button (4) to focus in on the tumor.
5) Click the "Start" button (5) to start the imaging process.
6) The superimposed brightfield and fluorescent images are shown over time (Fig.2).

Fig.2 The superimposed images are shown over the entire exposure period so an optimal image can be obtained even though the appropriate exposure time is unknown.

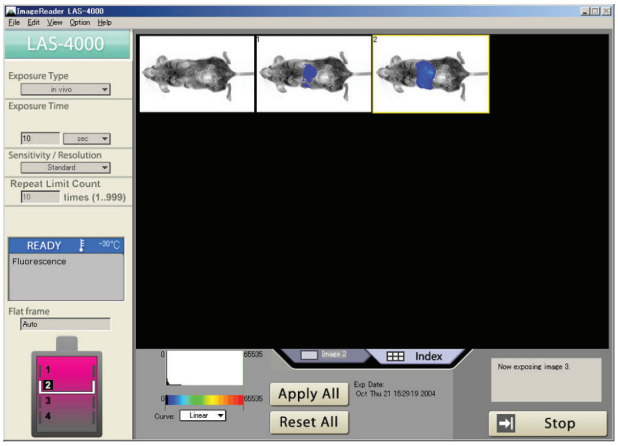

Fig.2

4 Results

Using near IR light and the IR785 long pass filter, the lesion within the tumor-bearing mouse was detected with high sensitivity and minimal background (Fig.3).

The superimposed image was generated automatically by using the "in vivo" mode within the LAS-4000 Image Reader software. Multiple images can be generated without changing the light source or the emission filters between captures (Fig.4). Also, because sequential images are stored over time, an optimal exposure can be obtained from the initial sample even though the signal intensity is unknown.

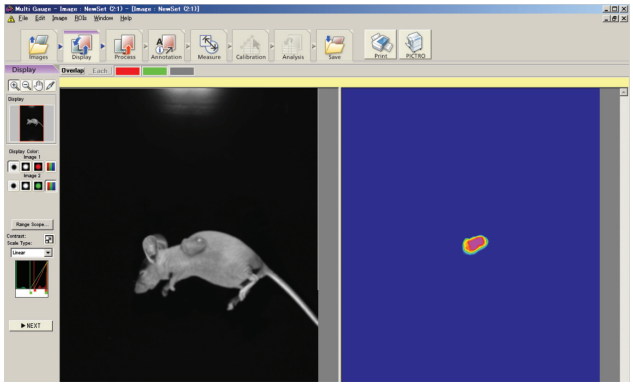

Fig.3

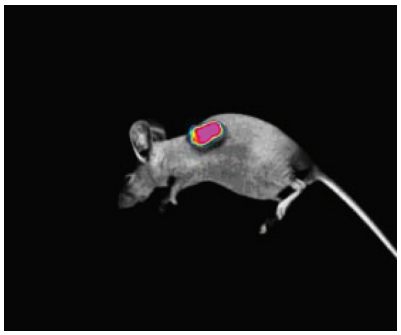

Fig.4

Fig.3 The image is displayed using "Multi Gauge Ver3.0" software. Quantitative data can be derived directly from the image

Detection conditions:
Digitize image (Left),
Light source … Incident white light,
Filter … Through,
Exposure time … 10 msec

IR image (Right),
Light source … Near-infrared (IR) light,
Filter … IR785,
Exposure time … 10 sec

Fig.4 The brightfield and near-infrared (IR) images are superimposed using "Multi Gauge Ver3.0" analysis software.

5 References

1) M Golzio, M-P Rols, B Gabriel and J Teisie, Optical imaging of in vivo gene expression : a critical assessment of the methodology and associated technologies, Gene Therapy 11, S85-S91, 2004.
2) Towards Imaging of Biological Function in Tissues and Whole Organisms, Takeharu Nagai, CELL TECHNOLOGY Vol.25 : 1010-1026, 2006.

Notice: With regard to patents owned by third parties related to, among other things, sample preparation, we recommend that you consult with a lawyer or patent attorney about obtaining a license from the third parties.

Data and protocol was supplied by Perseus Proteomics Inc. (Tokyo, Japan)

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EXHIBIT 2

EXHIBIT 2

FUJIFILM

Life Science

LUMINESCENT IMAGE ANALYZER

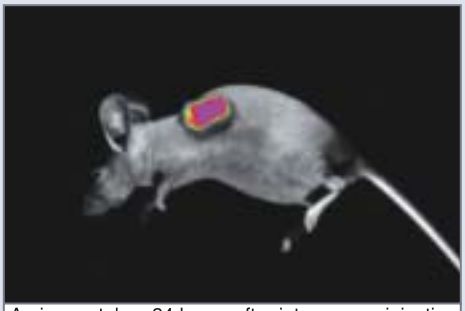
LAS-4000

The analyzer can be customized for detection methods selected from chemi/bioluminescence detection and a wide range of fluorescence detection by various light sources.

In addition to red, green and blue, near-infrared (IR) and ultraviolet (UV) epi-illuminators light sources are now available for your selection. The increased range of applicable reagents has expanded available applications. Near-infrared light, which is easily transmitted through tissues, enables high-sensitivity and high-resolution in-vivo imaging of small animal samples such as mice.

A free combination of light source options.

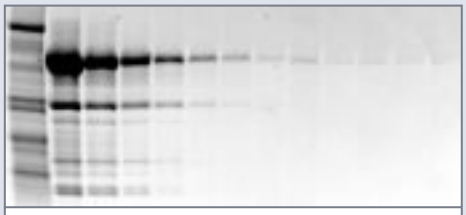
Multipul LED / IR, Red, Green, Blue, UV



An image taken 24 hours after intravenous injection of DY676-labeled antibody

Imaging parameters		
	Light source	: IR LED epi-illuminator
	Filter	: IR785
	Exposure time	: 10 seconds

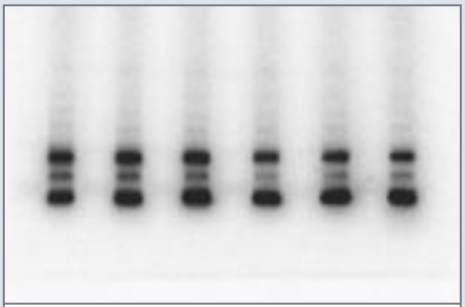
Multipul LED / Red, Green, Blue



Fluorescence detection of proteins by SYPRO®Ruby

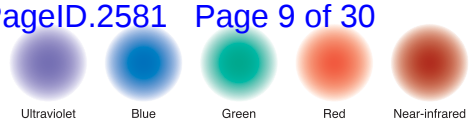
Imaging parameters		
	light source	: blue LED epi-illuminator
	filter	: Y515
	exposure time	: 3 seconds

Mono LED



Chemiluminescence detection of proteins by ECL Plus™

Imaging parameters		
	light source	: none
	filter	: none
	exposure time	: 60 seconds



Easy, rapid and sophisticated imaging with high sensitivity

The top-end model of the reliable, high-resolution LAS series has been designed more user-friendly than ever.

Remote control from a computer

Focus and diaphragm can be easily and rapidly controlled from the computer. By storing the imaging parameters employed at the previous detection, it saves on the time required for setting the parameters.

Quicker response to reduce stress

The system supports USB2.0 offering a high data-transfer rate. Quicker response to computer operation alleviates stress and improves efficiency.

Easy filter exchange

A filter changer mounted below the lens area can hold up to 4 filters at once. Filter selection can also be done from a computer.

User-friendly image capture software "LAS-4000 Image Reader" Mac® OS X 10.4.4 or later / Windows® XP Pro SP2 compatible

The self-explanatory and user-friendly software allows specification of all image capture parameters, including sensitivity, resolution and image methods. The software automatically carries out all image correction functions. In increment mode, the signal increase is shown in real time, by capturing and automatically displaying up to 16 images. With this software users can create their own settings and methods. A photograph of the sample can be made and overlaid with the signal image.


Method/Tray position Screen


Exposure Increment Screen

Large-aperture F0.85 lens

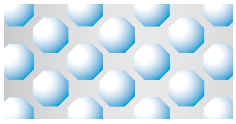
The analyzer incorporates a FUJINON, a strikingly bright lens with an F-number of 0.85. This lens has been especially designed to make full use of the advantages of Fujifilm's proprietary Super CCD chip, and is excellent for capturing images from distances as short as several tens of centimeters. In its design, optical expertise developed through professional applications such as broadcasting TV cameras lens is fully incorporated.


FUJINON LENS VRF43LMD3 F0.85

CCD affording up to 6.3 megapixels

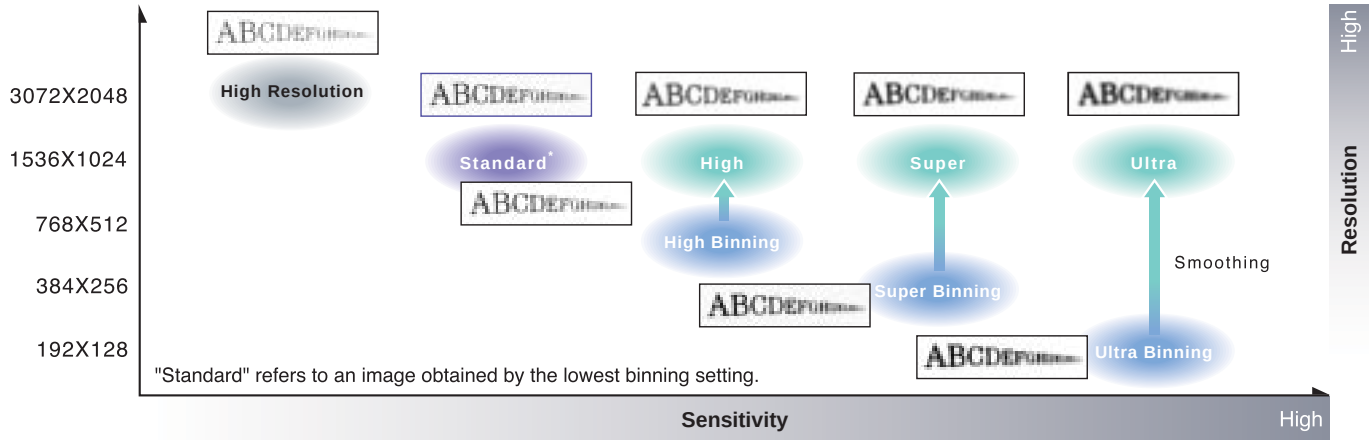
By rotating pixels 45 degrees to form an interwoven layout, the Super CCD's pixel pitch in the horizontal and vertical directions is narrower than in the diagonal direction, achieving higher horizontal and vertical resolution. This unique pixel layout design allows an image resolution with virtual 6.3 megapixels can be acquired by the Super CCD despite its real 3.2 megapixels.

Super CCD chip


Octagonal pixel-interwoven layout

Binning function enabling sensitivity improvement and smoothing

The four-stage binning function enables sensitivity improvement by one or more digits.
The resulting grainy image can be smoothed by selecting the smoothing mode.



A free combination of light sources can be incorporated into the analyzer according to your needs.
For example, the analyzer can be customized exclusively for luminescence detection, or for a wide range of fluorescence detection such as IR, UV.
Five epi-illuminator options (IR, red, green, blue and UV LEDs) and two transilluminator options (white and UV illuminators) are available.

◎Each epi-illuminator unit (IR, red, green, blue and UV) includes a white epi-illuminator. White epi-illuminator is included in all color illuminators.
◎The following models represent typical examples of light source combination. Any other combination is also available.
◎Light source types: Epi = incident light source, Dia = transmitted light source.

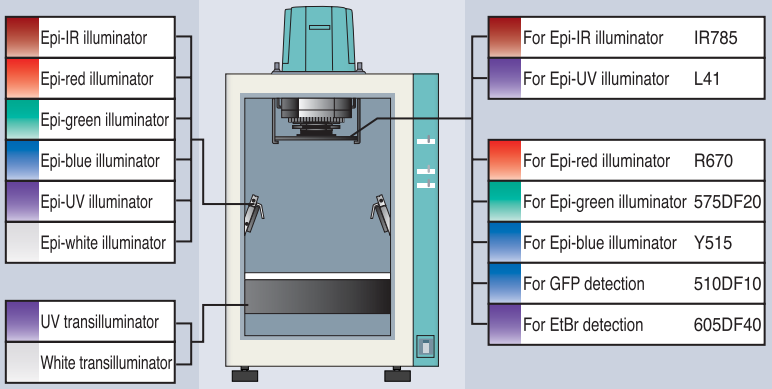
Light source | Filter | Detection method

Example combination 1

An all-rounder, covering from chemi/bioluminescence to in-vivo imaging.

IR, Red, Green, Blue, UV

Incorporates a full range of epi-illuminators, including "IR" and "UV" as well as "red/green/blue". Offers a wider range of fluorescence detection applications, such as in-vivo imaging using an IR illuminator.



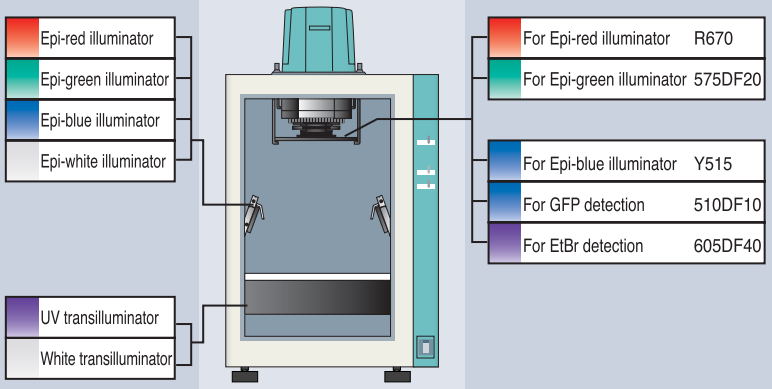
Luminescence
Chemiluminescence | Bioluminescence
Fluorescence
IR epi-illumination | Red epi-illumination
Green epi-illumination | Blue epi-illumination
UV epi-illumination | Trans-UV
Digitizing
White epi-illumination | White transillumination

Example combination 2

A multipurpose detector, covering from luminescence to RGB fluorescence.

Red, Green, Blue

Has satisfactory performance, function and total balance for accomplishing general imaging requirements, including chemi/bioluminescence detection, fluorescence detection by "red/green/blue" multicolor light sources and digitizing.



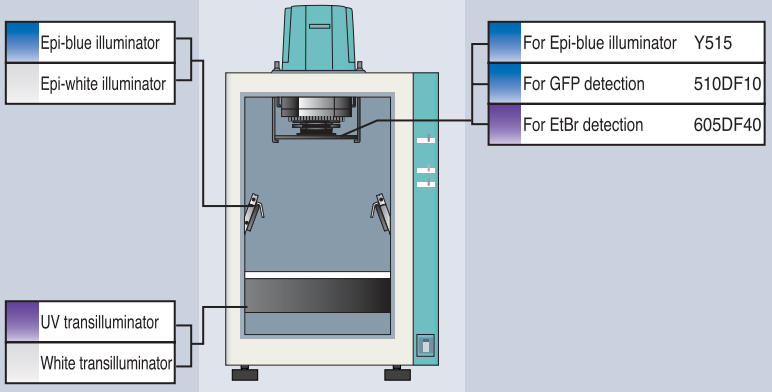
Luminescence
Chemiluminescence | Bioluminescence
Fluorescence
Red epi-illumination
Green epi-illumination | Blue epi-illumination
Trans-UV
Digitizing
White epi-illumination | White transillumination

Example combination 3

A single light source system focusing on chemi/bioluminescence detection.

Blue

A basic model with superior cost performance, optimized for those mainly performing chemi/bioluminescence detection. Incorporates blue epi-illuminator and UV transilluminator as light sources for fluorescence detection and is also capable of digitizing by white illuminator.



Luminescence
Chemiluminescence | Bioluminescence
Fluorescence
Blue epi-illumination
Trans-UV
Digitizing
White epi-illumination | White transillumination

Ultraviolet Blue Green Red Near-infrared

Applicable reagents

Luminescence

ECL™	ECL Plus™	ECL Advance™
Lumi-Light Plus	SuperSignal®	CDP-Star®
CSPD®	Immobilon	Bright-Star™

Fluorescence/IR

DY676	DY781
Alexa Flour® 680	Alexa Flour® 700

Fluorescence/red

Alexa Flour® 633	Alexa Flour® 635	Alexa Flour® 647
Cy™ 5	BODIPY® 650/665	DiD
TOTO® -3	DDAO phosphate	

Fluorescence/green

SYPRO® Red	Cy™ 3	TAMRA™
ROX™	HEX™	Alexa Fluor® 532
Alexa Fluor® 546	Deep Purple	Pro-Q® Diamond
Rhodamine Red™	BODIPY® 576/589	NED™
R-phycoerythrin	RFP	HNPP
Tetramethylrhodamine		

Fluorescence/blue

SYBR® Green I	SYBR® Green II	SYBR® Gold
SYPRO® Ruby	SYPRO® Orange	SYPRO® Tangerine
FITC	FAM™	EGFP
ECFP	AttoPhos™	

Fluorescence/epi-UV

Ethidium Bromide	SYPRO® Rose	Qdot®

Fluorescence/trans-UV

Ethidium Bromide

Digitizing/white epi-illumination/white transillumination

Silver staining	CBB	NBT/BCIP
X-ray film, etc.		

*** The reagents listed above are representative reagents with high performance results. Please contact us for other reagents.**

Bioimaging by near-infrared light (using epi-IR/white LED)

A tumor in nude mouse was detected by antibody* labeled with DY676, a near-infrared fluorescent dye. The image was obtained 24 hours after antibody intravenous injection. The near-infrared fluorescence image was overlapped with the digitized image and analyzed using standard analysis software.

*antibody : an antibody directed against a human cancer cell surface marker was supplied by Perseus Proteomics Inc.

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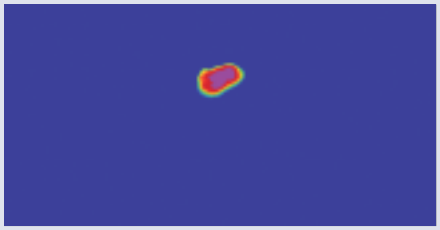
Near-infrared fluorescence image



Near-infrared fluorescence detection of DY676-labeled antibody distribution.

Light source: epi-IR illuminator	Filter: IR785	Exposure time: 10 seconds

Digitized image

Digitized image of a living mouse

Light source: epi-white illuminator	Filter: none	Exposure time: 0.01 seconds

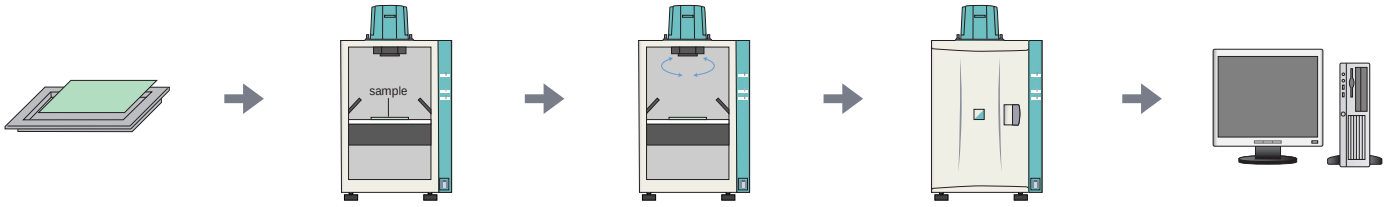
Overlapped image

The two images were overlapped using "MultiGauge (Science Lab)" to enable easy quantitative analysis of DY676-labeled antibody distribution.

External cable/tube insertion port

The analyzer has a port for inserting temperature adjustment/anesthesia cables and tubes.

Analysis procedures using LAS-4000



Place sample on the tray | Load the tray | Remote focusing | Exposure | Analysis

Specifications and Configuration

Image Capturing Unit (Requires additional Analyzing Unit)

- **Camera head**

CCD chip	: Fujifilm Super CCD Area Type chip(15.6 x 23.4mm)
Number of pixels	: 3.2 million pixels
Pixel size	: Approx. 11 μm
Cooling	: Two-stage thermoelectric module with air circulation
Cooling temperature	: Down to -30℃ (When room temperature is below 28℃.)
Dynamic range	: Four orders of magnitude
Focusing and diaphragm	: Automatic, remote operation
Gradation	: 16 bits
Exposure mode	: Automatic / manual (normal / incremental / repetitive / program / invivo)
Exposure time	: Automatic / manual (1 / 100 seconds to 30 hours)
Pixel correction	: Dark-frame correction, flat-frame correction, distortion correction, etc.
Image quality correction	: Binning and smoothing
Image size	: Up to 12 MB (formats : FUJI and TIFF)
Read pixel size	: Down to 35 μm
Maximum sample size	: 21 x 14 cm (25 x 25 cm when using a wide-view lens)
Interface	: USB 2.0

- **Intelligent Dark Box Set**
  Includes; IDX box, Epi-tray, USB Cable.
- **Lens**
  High-sensitivity lens : FUJINON Lens VRF43LMD 3
  SIGMA Wide-view Lens is also available.
- **Operating conditions**

Line frequency	: 50 - 60 Hz
Temperature	: 15 - 28 ℃
Humidity	: 30 - 70% (no condensation)
Supply Voltage	: 100 - 240V
Power Consumption	: Approx. 0.3 kVA

- **Dimensions**
  Camera head and dark box : 510 (W) x 900 (H) x 480 (D) mm

Optional Products*

- **UV 2020 Transilluminator set**
  Includes; UV Transilluminator(312nm), Gel sheet, UV Dia-tray, 605DF40 filter.
- **White Transilluminator(470~740nm) set**
  Includes; White Trans-illuminator, White Dia-tray
- **Epi-Blue Illuminator set**
  Includes; Epi-Blue(460nm) / White Illuminator, Y515 filter.
- **Epi-Green Illuminator set**
  Includes; Epi-Green(520nm) / White Illuminator, 575DF20 filter.
- **Epi-Red Illuminator set**
  Includes; Epi-Red(630nm) / White Illuminator, R670 filter.
- **Epi-IR Illuminator set**
  Includes; Epi-IR(710nm) / White Illuminator, IR785 filter.
- **Epi-UV Illuminator set**
  Includes; Epi-UV(365nm) / White Illuminator, L41 filter.
- **UV Dia-tray set**
  Includes; UV Dia-tray, Gel sheet
- **Non-parallax tray**
- **Optical Filter: Y515**
  510DF10 for GFP detection
  605DF40 for EtBr detection
- **Filter changer**

* Each light source set includes filter(s) for the corresponding wavelength range(s).
The three optional filters can be purchased individually.

Analyzing Unit (separate product)

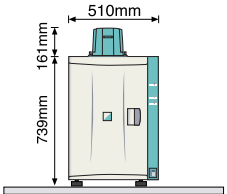
- **Computer**
  OS : Mac® OS X 10.4.4 or later
  Windows® XP Pro SP2
- **Analysis software** : ScienceLab

Remarks

- **Gel documentation is available by digitizing**
- An optimum system for meeting your needs can be constructed by freely combining a wide array of options with the basic model*

* Basic model: Camera Head + Intelligent Dark Box set + Lens

< Image capturing unit >



- The desk is not included.
- The maximum depth is approximately 500 mm.
- The figure above represents a model loaded with the UV illuminator .

< Analyzing unit >

● excitation light source units*
blue LED epi-illuminator, green LED epi-illuminator, red LED epi-illuminator, ultraviolet (UV) LED epi-illuminator, near-infrared (IR) LED epi-illuminator
* Each of the epi-illuminator units for different wavelengths includes a white epi-illuminator.
White epi-illuminator is included in all color illuminators.

● various filters
510DF10* for GFP detection, Y515* for yellow or red fluorescence detection, 605DF40* for EtBr detection, 575DF20 for orange fluorescence detection, R670 for dark red fluorescence detection, IR785 for IR detection, L41 for visible fluorescence detection
* available as options also

http://lifescience.fujifilm.com

LAS-4000 (with any Epi-illuminator) is categorized as the class 1 laser (LED) (IEC60825-1+A2:2001).

Notice: With regard to patents owned by third parties related to, among other things, sample preparation, we recommend that you consult with a lawyer or patent attorney about obtaining a license from the third parties.

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EXHIBIT 3

EXHIBIT 3

(MS) can be used to detect the presence of LK derivatives in very small quantities, however, MS is very time consuming and requires expensive equipment and a highly trained operator.

ECD plays a key role

This helps explain why ECD has become such a popular method of measuring biological and clinical molecules. ECD detectors work by applying a voltage between a working and a reference electrode in a flow cell. As molecules pass through the flow cell, those that can be easily oxidized or reduced at the applied potential react at the working electrode, producing a flow of electrons. The detector measures this flow. Only those molecules that will oxidize or reduce at the electrode at the applied potential are detected, thus providing a high degree of selectivity. The inherent sensitivity, selectivity, and wide dynamic range of this technique have caused it to be used extensively in brain research and other areas of medical research.

Up to now, noble metals such as silver and platinum and various forms of carbon have been used as ECD electrodes. In particular, carbon-based electrodes have found extensive use in a broad range of applications. These electrodes are limited in the molecules they can detect because of restrictions in the potential ranges that can be used with these electrodes. These restrictions arise as a result of water electrolysis at conventional electrodes; at positive potentials, water decomposes to form oxygen, and hydrogen forms at negative potentials, leaving a window of only approximately one volt with which to oxidize or reduce analytes. This window is too narrow to identify LK variants.

A key advantage of boron doped diamond electrodes is that they open up the potential window to between three and four volts, sufficient to detect LK and its variants.

Boron-doped diamond electrodes extend ECD

"Diamond, in its natural state, is unsuitable for use as an electrode because of its inertness. However, methods have been developed for including metal dopants in diamond films that render the inherently insulting diamond film conductive.

Boron-doped diamond electrodes are typically constructed on a supporting substrate, most often silicon or a metal. The polycrystalline thin film is formed by chemical vapor deposition. At high levels of boron doping, diamond becomes highly conductive, making it a suitable electrode material. A key advantage of boron-doped diamond electrodes is that they open up the potential window to between three and four volts, sufficient to detect LK and its variants, many other thiols

The boron-doped diamond electrodes when used in an ESA amperometric cell can operate over a greater potential range than traditional carbon electrodes, making more molecules amenable to detection. Molecules such as LK and its variants, as well as many other thiols and disulfides, can be detected with the BDD electrode. (Source: ESA Biosciences)

Huntington's disease is believed to damage nerve cells through inflammation, excess nitric oxide production, and excess glutamate excitotoxicity. The OMRF researchers focused on LK and its derivatives because they have antioxidant, antineuroinflammatory, and neuroprotective properties. Scientists have been conducting laboratory tests with LK, and early data indicates the compound could stop damage to nerve cells and reduce inflammation. Doing so would delay the motor-function deterioration caused by Huntington's disease.

Reaching brain cells is key to search for treatment

A key challenge in developing a compound for treatment or prevention of this disease is improving the delivery of LK derivatives to target brain cells and particularly improving permeability through the blood-brain barrier. The OMRF researchers are working to improve delivery through derivatization of LK to form LK esters (LKEs) and LK amides (LKAs). For example LK ethyl ester has proven more capable of penetrating cell membranes and reaching intracellular targets of action.

A critical aspect of improving the delivery of LK derivatives involves the ability to accurately measure them at very low concentrations in the brain of animals used in research. Nervous system cells contain many different components that must usually be separated before they can be analyzed and quantitated. High performance liquid chromatography (HPLC) provides an excellent separation tool. Mass spectrometry

EXHIBIT 4

EXHIBIT 4

FUJIFILM

Life Science

Optional Kit for LAS-4000

LAS in vivo Assist Kit

Easy installment on your LAS-4000 and easy connection to anesthesia equipment
The LAS in vivo Assist Kit enables you to become more familiar with biogenic images

LAS in vivo Assist Kit

Anesthetic Manifold supports the anesthetizing of small animals

Exclusive heat control prevents hypothermia of anesthetized small animals

Easy maintenance using removal and washable Anesthetic Manifold

Easy connection to anesthesia equipment

By connecting to anesthesia equipment, isoflurane can be used.
Inserting the port tube and the anesthetic manifold supports the anesthetizing of small animals.

Exclusive manifold

Exclusive manifold enables maintenance of the anesthetized condition using isoflurane.
After drug administration, the manifold allows observation of kinetic analysis for a long period of time (a mouse was under anesthesia for one hour and normal arousal condition was validated).

The exclusive heat control

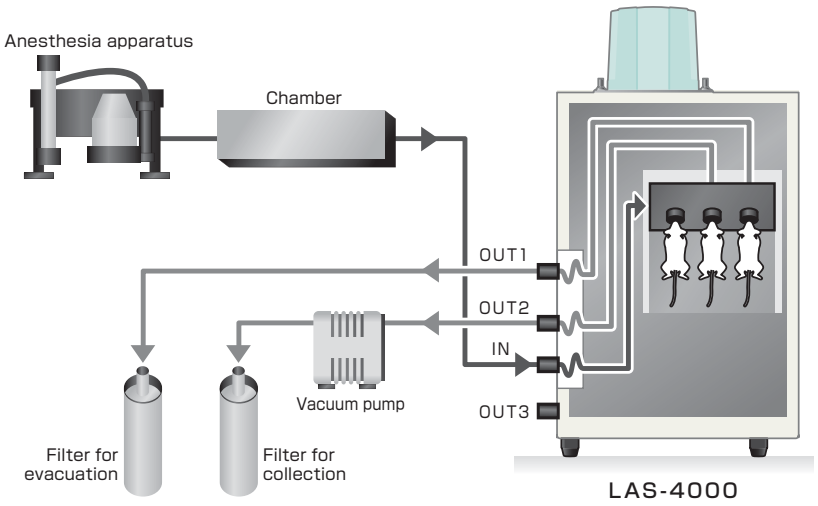
The exclusive heat control prevents hypothermia of anesthetized small animals by keeping the temperature at a constant 37℃ (tested while room temperature was at 25℃).

Compatible with LAS-4000

No need to purchase additional in vivo imaging equipment.
Easy installment on your LAS-4000 and after installation, the basic function of the equipment stays the same. Imaging light sources, such as Gel & Membrane images can be captured.

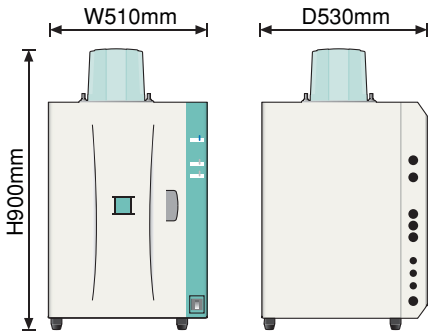
*The feature of isoflurane :
Rapid induction and arousal with strong anesthesia effect.
No risk of hepatotoxicity, nephrotoxicity and cardiac arrhythmia.
Very low risk of myocardial contraction.
Use of isoflurane is safer than anesthesia injection (e.g. Nembutal).

Reference piping arrangement



※Please install this kit at well ventilated place.
※This product is only for Isoflurane.
※Anesthesia system is not included.

Image capturing unit



Composition

LAS in vivo Assist Kit

- Door frame
  456×696×80 mm (W/H/D), 4.5kg (excluding the protruding parts)
- Manifold
- Body heat retention tray
  328×63×306 mm (W/H/D), 2.5kg (including the gas manifold)
- Heater controller box
  322×86×313 mm (W/H/D), 3.0kg (excluding the protruding parts)
- Operation Manual

http://lifescience.fujifilm.com

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EXHIBIT 5

EXHIBIT 5

eXplore Optix

Pre-clinical Optical Imaging System

Fluorescence Imaging for *In-vivo* applications

imagination at work

eXplore Optix

Pre-clinical Optical Imaging System

GE Medical Systems
100 Collip Circle, Suite 120
London, Ontario N6G4X8

Toll Free 888.725.8285

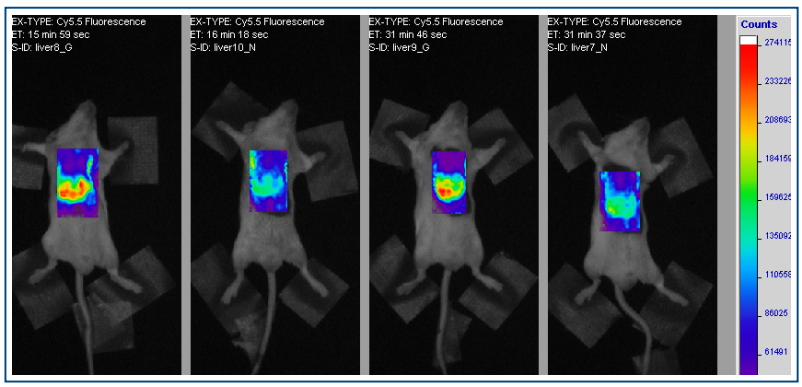
http://gemedical/preclinical_imaging

Product Specifications

Overview

eXplore Optix has been designed to characterize, quantify and visualizes cellular and molecular events in living animals using specific or non-specific fluorescent probes . Non-invasively tracking these events in vivo can dramatically improve the quantity and quality of research information, expedite drug discovery and development, and significantly reduce the cost of animal research.

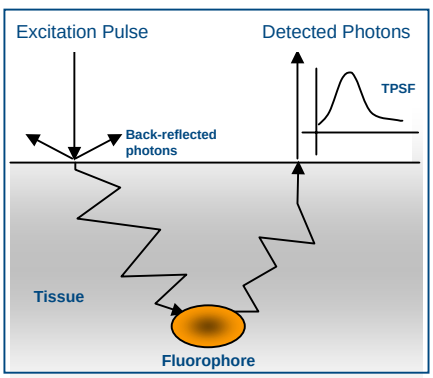
eXplore Optix, *In-vivo* molecular imaging allows longitudinal studies to be conducted in the same animal. Following a single animal over time allows researchers to more accurately measure the effect of intervention, disease progression and outcome. This ultimately results in more specific and earlier disease diagnosis as well as improved treatment monitoring.



The images above depict uptake of a targeted versus non-targeted agent at two time-points

Technology

eXplore Optix uses a time-correlated single photon counting(TCSPC) technique to measure fluorescence and absorption. This technique measures photon migration of short pulses of light at specific wavelengths. The arrival time distributions, or temporal point spread function (TPSF), are detected and then used to derive and separate absorption and scattering coefficients, quantify the fluorescence emitter, and provide fluorescent lifetime.



Advantages

- Provides accurate **localization** of embedded fluorescent material.
- Temporal information enables the system to quantify inclusion **depths**.
- Through depth, temporal information leads to an accurate estimate of fluorophore **concentration**.
- Measuring **fluorescence lifetime** allows distinction between different fluorescent materials.

imagination at work

eXplore Optix

Pre-clinical Optical Imaging System

GE Medical Systems
100 Collip Circle, Suite 120
London, Ontario N6G4X8

Toll Free 888.725.8285

http://gemedical/preclinical_imaging

Product Specifications

ILLUMINATION SYSTEM	Pulsed laser diode
▪ Laser Repetition rate	80 MHZ
▪ Pulse width	< 100 ps
▪ Excitation wavelength[1]	600 - 900 nm
▪ Illumination spot	1 mm on major axis
DETECTION SYSTEM	Time correlated single photon counting system
▪ Detector	PMT (photomultiplier tube)
▪ Temporal resolution	250 ps
▪ Depth Sensitivity	>10mm at 700nm
▪ Detection wavelengths1	450 - 900 nm
▪ Detection spot	1 mm diameter
SPATIAL RESOLUTION	0.5 - 3 mm steps
ANIMAL PLATE	Removable, adjustable height
▪ Size	20 x 9 cm
▪ Temperature setting	Adjustable range 26 - 42°C
ENCLOSURE	Light tight
▪ Dimensions	114 x 76 x 84 cm (L x W x H)
▪ Weight	90 kg
▪ Ports for inhalation anesthetic	
SCANNING PRINCIPLE	Raster scanning
▪ Longitudinal	Linear translation stage
▪ Transversal	1 galvanometer for scanning detection spot 1 galvanometer for scanning illumination spot
SCAN AREA	20 x 8.4 cm
▪ Region of interest (ROI)	Any size ROI within selected scan area
SCAN TIME	0.3 - 1 sec. collection at each point in ROI

[1]Refer to Table 1 for available laser diode configurations

Rev 0

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eXplore Optix

Pre-clinical Optical Imaging System

GE Medical Systems
100 Collip Circle, Suite 120
London, Ontario N6G4X8

Toll Free 888.725.8285

http://gemedical/preclinical_imaging

Product Specifications

MEASUREMENT CAPABILITIES — Intensity, Fluorescence lifetime, & absorption

SOFTWARE — Automated data acquisition, image processing,and display and image analysis.

COMPUTER

- Processor — 2.4Ghz or better Pentium 4
- Memory — 256 MB DDR RAM
- Disk — 40 GB Hard drive
- Monitor — 17” or 18" LCD Flat Panel
- Operating System — Windows 2000 (Service Pack 3)

ELECTRICAL — Universal power supply (120 or 240 VAC)

Table 1: Available Laser Diode Configurations

Catalog	Excitation Wavelength	Emission Wavelength	Example Fluorophore
P2000PK	670 nm	700 nm	Cy5[2], Cy5.5[2] Alexa Fluor 680[3]
P2000PL	750 nm	780 nm	Cy7[2] Alexa Fluor 750[3]
P2000PM	630 nm	650 nm	BODIPY[3]

[2] **Amersham Bioscience**
[3] **Molecular Probes**
[4] **Sigma-Aldrich**

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EXHIBIT 6

EXHIBIT 6

GE Healthcare

eXplore Optix

in vivo fluorescence optical imaging system

Time-domain fluorescent imaging

Near-infrared imaging
Breadth of applications

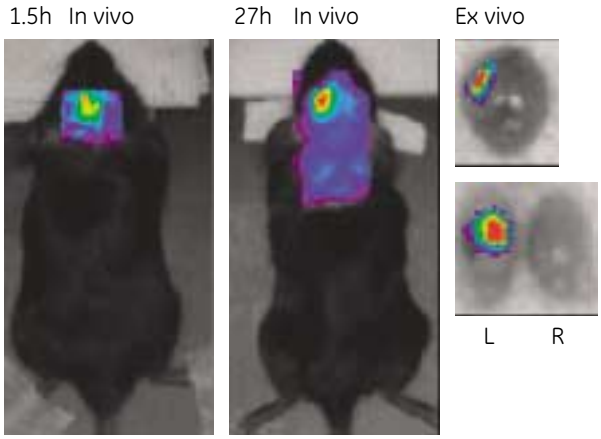
Fluorophore quantification
High content data

Integrated, multi-modality platform
Quantitative 3-D data

eXplore Optix is a high performance in vivo fluorescence optical imaging system designed to characterize, quantify and visualize cellular and molecular events in living animals using specific or non-specific fluorescent probes. Using a proprietary time domain (TD) approach, eXplore Optix can be applied to further understand the mechanism of disease and evaluate the effects of therapy and disease progression.

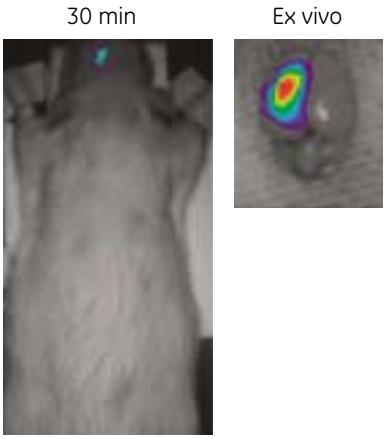
eXplore Optix offers:

- **Near-infrared imaging (NIR)** - Allows deep penetration of light due to its low tissue absorption.
- **Fluorophore quantification** - Quantitative measures of fluorophore intensity, relative concentration, depth, and fluorescence lifetime for improved data and analysis, including 3-D image reconstruction.
- **Integrated, multi-modality platform** - Simultaneously monitor biodistribution of multiple biological targets, perform co-registration with in vivo microCT for improved anatomical reference, then seamlessly export DICOM images to clinical workstations to improve productivity.



In vivo optical imaging of the blood-brain barrier permeability in C57Bl mice subjected to a 60-min left middle cerebral artery occlusion (MCAO) and indicated reperfusion times. Ex vivo imaging confirms the origin of the signal from the left hemisphere.

Source: National Research Council of Canada, Dr. Ed Preston.



In vivo optical imaging of increased blood to brain diffusion of a fluorescent probe observed 30 minutes after unilateral chemical opening of the blood-brain barrier in the left hemisphere in the anesthetized rat. Ex vivo imaging confirms the origin of the signal from the left hemisphere.

Source: National Research Council of Canada, Dr. Ed Preston.

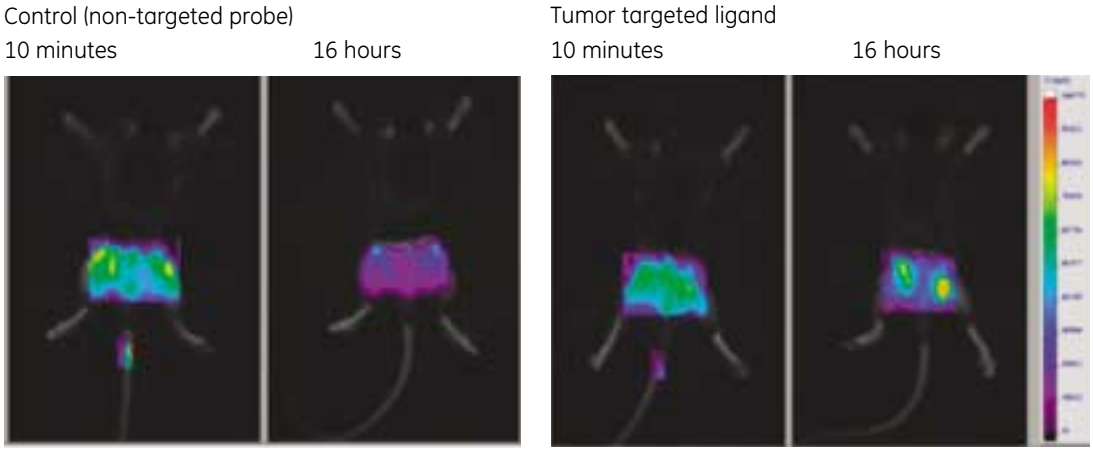
NIR imaging for a breadth of applications

Imaging cell surface antigens

Several cell surface receptor molecules can be over-expressed on activated endothelial cells and tumor cells. Their ligands or peptides with high specificity can be labeled with fluorescent dyes and used for tumor imaging.

Other applications:

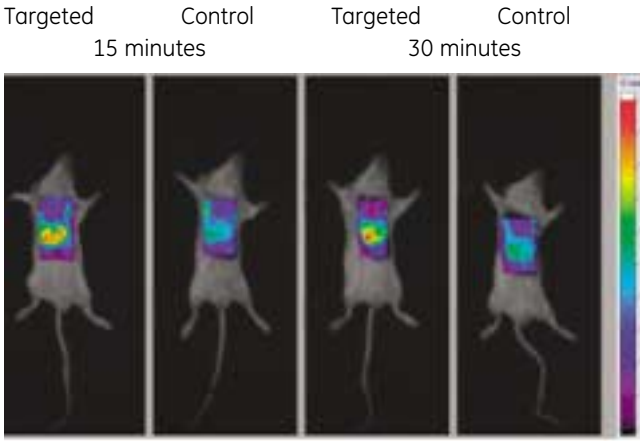
- **Intra and extra cellular environments:** Using the lifetime decay properties of a given fluorophore, differentiate between fluorophore environments
- **Reporter genes:** Monitor cellular events associated with signal transduction, gene expression and protein-protein interactions



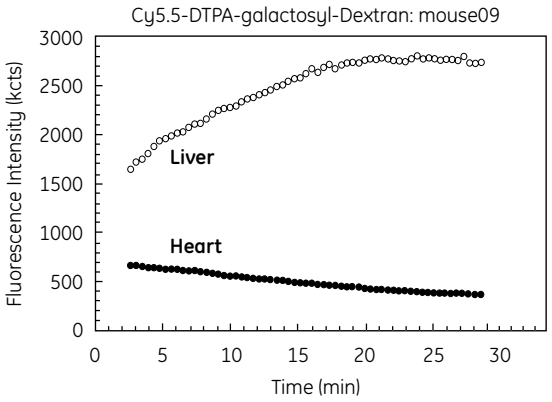
Imaging of tumor-specific antigens following I.V. injection of probe. After 10 minutes, high levels of background fluorescence are apparent in both animals. After 16 hours, high levels of labeling are evident in the animal injected with the tumor targeted probe.

Pharmacokinetics

Therapeutic intervention can be longitudinally monitored in a small cohort of experimental animals.



Example of a pharmacokinetics study using Cy5.5 dye that was covalently linked to both DTPA-galactosyl-dextran (liver receptor targeted compound) and to DTPA-dextran (control compound) to evaluate hepatic uptake.



Time-activity plot of this pharmacokinetics study showing how the liver exhibits rapid uptake and accumulation, whereas the heart displays rapid clearance in the targeted animal.

Source: David R. Vera, Ph.D., University of California, San Diego, Medical Center

Fluorophore quantification for depth and concentration

eXplore Optix technology

Any optical imaging solution must overcome the physical principles that impact optical signal intensity, including the scattering and absorption characteristics of surrounding tissue and background noise such as auto-fluorescence. Due to these confounding factors, the utility of the intensity signal may not be sufficient for applications requiring quantification.

eXplore Optix overcomes these limitations and provides precise measurements of fluorophore intensity, concentration and 3-D localization.

Based on a time-domain approach, eXplore Optix uses short pulses of narrow-spectrum light driven by pulsed laser diodes for excitation. To capture the arrival time distribution of the emitted fluorescent photons (temporal point spread function, or TPSF), eXplore Optix uses a single photon counting photo-multiplier tube. This approach allows tissue depth to be determined and factored into attenuation correction calculations to provide accurate, relative fluorophore concentration.

Fluorescence lifetime

Due to the nanosecond temporal time resolution of eXplore Optix, investigators can obtain in vivo fluorescence lifetime measurements to discriminate fluorophores with similar spectral profiles. In addition, with the use of probes these investigators can identify microenvironment changes in pH, oxygen level, temperature and other factors known to affect fluorescence lifetime.

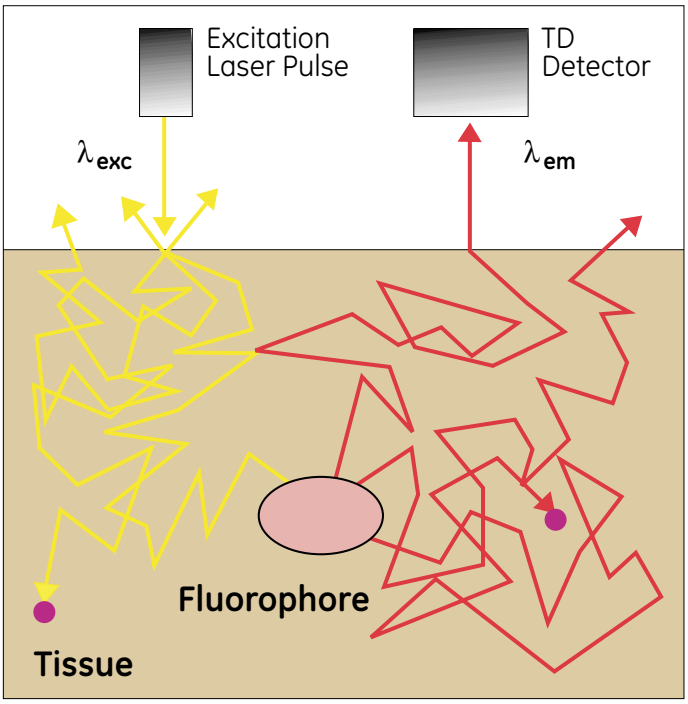


Diagram showing the path of the fluorescent photons after emission from eXplore Optix.

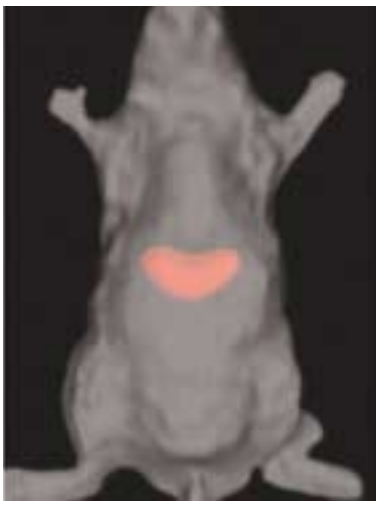
Integrated multi-modality platform for quantitative 3-D data

3-D multi-modality image fusion
eXplore Optix shares an animal bed with Locus (pre-clinical CT) to enable multi-modality image fusion. Its automated registration and visualization software tools speed the fusion process to streamline workflow. By combining the high sensitivity of eXplore Optix with the high resolution of eXplore Locus, fluorescent tracers can be detected, quantified, monitored and registered to a specific 3-D location.

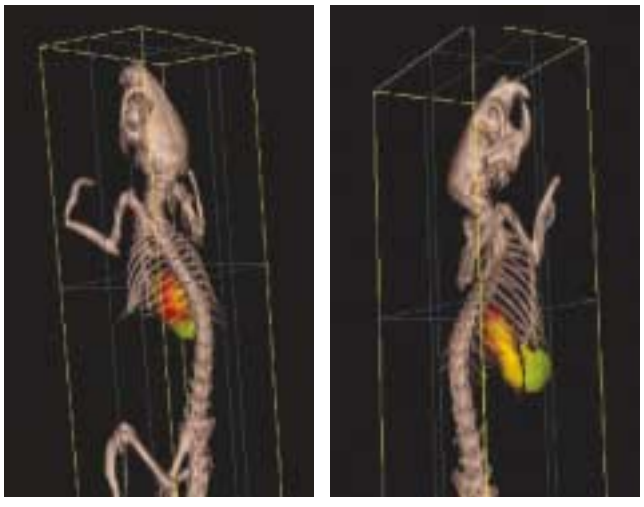
Tomography
Time-domain optical imaging permits high sensitivity depth probing and tomography from a planar imaging geometry.

Multi-wavelength
Multi-wavelength excitation significantly extends the operating spectrum and flexibility of eXplore Optix by supporting up to four pulsed laser diodes and up to 14 filters. With the additional laser diodes and filters, multiple fluorescent targets with different spectral properties extending from the visible to NIR spectrum can be utilized.

A dedicated partner
For researchers across the globe, GE Healthcare is the partner of choice due to our core capabilities in diagnostic imaging and our expertise in biology and chemistry. In addition, we provide regionally based service and application training teams to maintain systems on-site and provide ongoing technical support.



3-D tomography image



Examples of co-registration with an eXplore Locus uCT scanner.

eXplore Optix was developed and is manufactured by Advanced Research Technologies, Inc. (ART)

GE Medical Systems, a General Electric company, going to market as GE Healthcare.

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